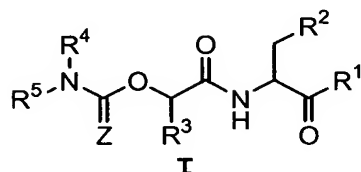


CLAIM AMENDMENTS

1-21. (canceled)

22. (currently amended) A compound of formula **I**:



wherein:

Z is oxygen or sulfur;

R¹ is hydrogen, -CHN₂, -R, -CH₂OR, -CH₂SR, or -CH₂Y;

R is a C₁₋₁₂ aliphatic, aryl, aralkyl, heterocyclyl, or heterocyclylalkyl ring, wherein each of these groups is optionally substituted, and wherein said heterocyclic ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S;

Y is an electronegative leaving group selected from F, Cl, Br, I, arylsulfonyloxy, alkylsulfonyloxy, trifluoromethanesulfonyloxy, OR', SR', -OC=O(R'), or -OPO(R⁶)(R⁷);

wherein R' is an aliphatic group, an aryl group, an aralkyl group, a carbocyclic group, an alkyl carbocyclic group, a heterocyclic group, or an alkyl heterocyclic group;

wherein R⁶ and R⁷ are independently selected from R or OR;

R² is: ~~CO₂H, CH₂CO₂H, or esters or amides or isosteres thereof,~~

i) CO₂H, or an ester, or an amide thereof; or R² is an isostere of said CO₂H; or

ii) CH₂CO₂H, or an ester, or an amide thereof; or R² is an isostere of said CH₂CO₂H;

~~R³ is a group capable of fitting into the S2 sub site of a caspase; and~~

selected from H, a side chain of a natural α-amino acid, or a substituted or unsubstituted group having a molecular weight up to about 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl or heterocyclylalkyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and

R⁴ and R⁵ taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system having 1-6 heteroatoms selected from nitrogen, oxygen or sulfur;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R⁹, -OR⁹, -OH, -SH, -SR⁹, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO₂, -CN, -NH₂, -NHR⁹, -N(R⁹)₂, -NHCOR⁹, -NHCONHR⁹, -NHCON(R⁹)₂, -NR⁹COR⁹, -NHCO₂R⁹, -CO₂R⁹, -CO₂H, -COR⁹, -CONHR⁹, -CON(R⁹)₂, -S(O)₂R⁹, -SONH₂, -S(O)R⁹, -SO₂NHR⁹, or -NHS(O)₂R⁹;

wherein each R⁹ is independently selected from an aliphatic group or a substituted aliphatic group;

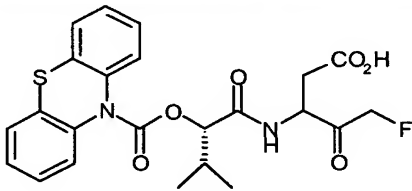
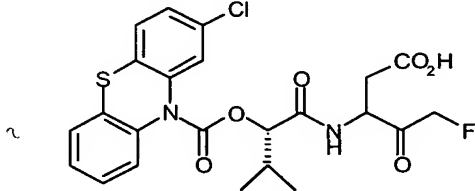
wherein the optional substituents on said C₁₋₁₂ aliphatic group or aryl, aralkyl, heterocyclyl, or heterocyclylalkyl ring is independently selected from,

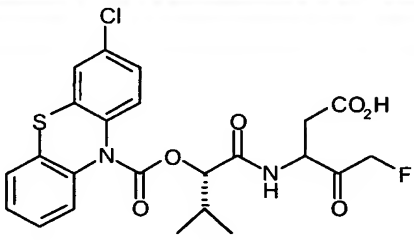
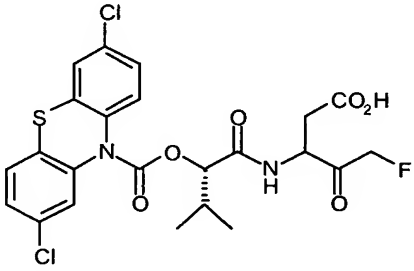
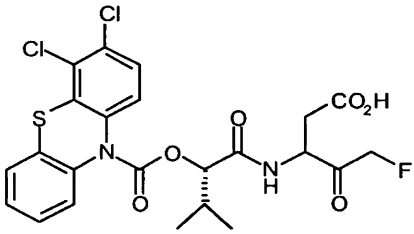
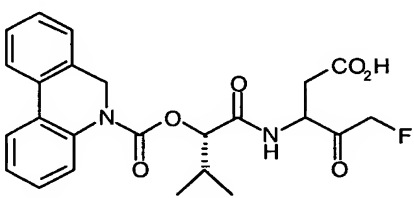
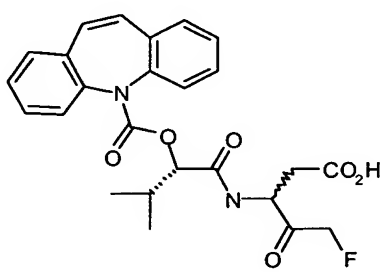
from halogen, $-R^{11}$, $-OR^{11}$, $-OH$, $-SH$, $-SR^{11}$, acyloxy, substituted or unsubstituted Ph or OPh, $-NO_2$, $-CN$, $-NH_2$, $-NHR^{11}$, $-N(R^{11})_2$, $-NHCOR^{11}$, $-NHCONHR^{11}$, $-NHCON(R^{11})_2$, $-NR^{11}COR^{11}$, $-NHCO_2R^{11}$, $-CO_2R^{11}$, $-CO_2H$, $-COR^{11}$, $-CONHR^{11}$, $-CON(R^{11})_2$, $-S(O)_2R^{11}$, $-SONH_2$, $-S(O)R^{11}$, $-SO_2NHR^{11}$, $-NHS(O)_2R^{11}$, $=O$, $=S$, $=NNHR^{11}$, $=NNR^{11}_2$, $=N-OR^{11}$, $=NNHCOR^{11}$, $=NNHCO_2R^{11}$, $=NNHSO_2R^{11}$, or $=NR^{11}$; and

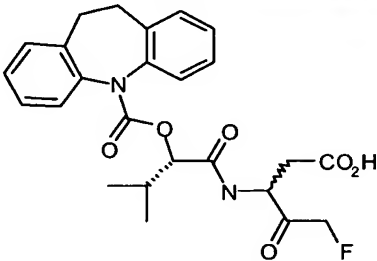
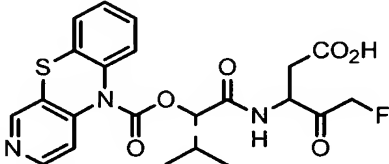
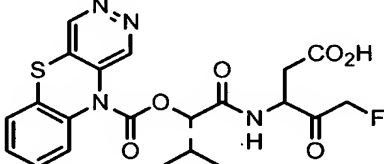
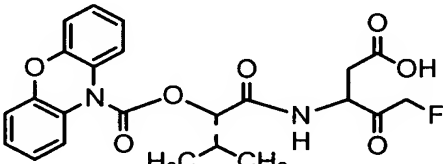
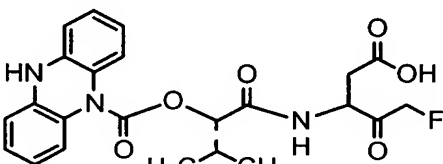
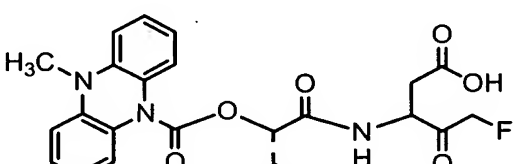
wherein each R^{11} is independently selected from a C_{1-12} aliphatic group or a substituted C_{1-12} aliphatic group.

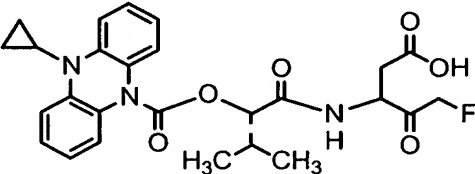
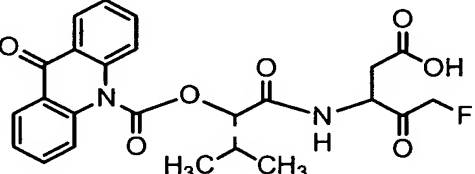
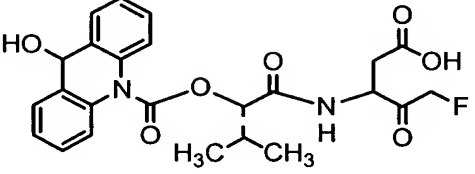
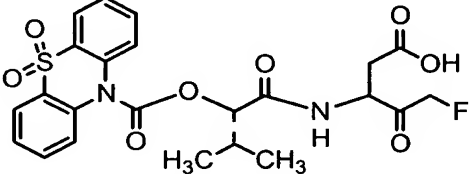
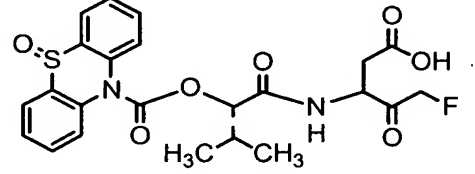
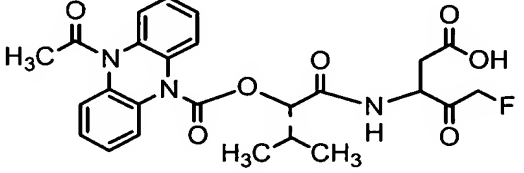
23-35. (canceled)

36. (currently amended) The compound of claim 22 wherein the compound is selected from those compounds listed in Table 1 below:

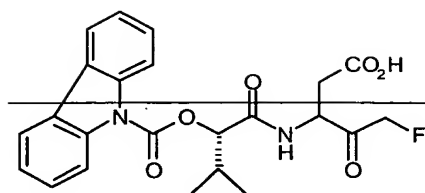
No.	Structure
12	
13	

No.	Structure
14	
15	
16	
17	
18	

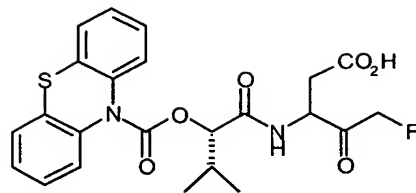
No.	Structure
19	
38	
39	
40	
41	
42	

No.	Structure
43	
44	
45	
46	
47	
48	

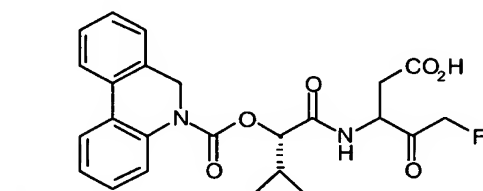
37. (currently amended) The compound of claim 22 wherein the compound is selected from the following:



11



12



17

38. (canceled)

39. (new) The compound according to claim 22 wherein Z is oxygen.

40. (new) The compound according to claim 22 wherein R¹ is hydrogen, -R, -CH₂OR, -CH₂SR, or -CH₂Y.

41. (new) The compound according to claim 22 wherein R² is:

CO₂H, or an ester, or an amide thereof; or R² is an isostere of said CO₂H.

42. (new) The compound according to claim 22 wherein R³ is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring

system wherein each ring contains up to three heteroatoms selected from O, N, or S.

43. (new) The compound according to claim 22 wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$, $-CO_2R^9$, $-CO_2H$, $-COR^9$, $-CONHR^9$, $-CON(R^9)_2$, $-S(O)_2R^9$, $-SONH_2$, $-S(O)R^9$, $-SO_2NHR^9$, or $-NHS(O)_2R^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

44. (new) The compound according to claim 22 wherein Z is oxygen; and wherein R^1 is hydrogen, $-R$, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$.

45. (new) The compound according to claim 22 wherein Z is oxygen; and wherein R^2 is:

- i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or
- ii) CH_2CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CH_2CO_2H .

46. (new) The compound according to claim 22 wherein Z is oxygen; and wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

47. (new) The compound according to claim 22 wherein Z is oxygen; and wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$, $-CO_2R^9$, $-CO_2H$, $-COR^9$, $-CONHR^9$, $-CON(R^9)_2$, $-S(O)_2R^9$, $-SONH_2$, $-S(O)R^9$, $-SO_2NHR^9$, or $-NHS(O)_2R^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

48. (new) The compound according to claim 22 wherein R^1 is hydrogen, $-R$, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$; and wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or

ii) $\text{CH}_2\text{CO}_2\text{H}$, or an ester, or an amide thereof; or R^2 is an isostere of said $\text{CH}_2\text{CO}_2\text{H}$.

49. (new) The compound according to claim 22 wherein R^1 is hydrogen, $-\text{R}$, $-\text{CH}_2\text{OR}$, $-\text{CH}_2\text{SR}$, or $-\text{CH}_2\text{Y}$; and wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

50. (new) The compound according to claim 22 wherein R^1 is hydrogen, $-\text{R}$, $-\text{CH}_2\text{OR}$, $-\text{CH}_2\text{SR}$, or $-\text{CH}_2\text{Y}$; and wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-\text{R}^9$, $-\text{OR}^9$, $-\text{OH}$, $-\text{SH}$, $-\text{SR}^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-\text{OPh}$, substituted $-\text{OPh}$, $-\text{NO}_2$, $-\text{CN}$, $-\text{NH}_2$, $-\text{NHR}^9$, $-\text{N}(\text{R}^9)_2$, $-\text{NHCOR}^9$, $-\text{NHCONHR}^9$, $-\text{NHCON}(\text{R}^9)_2$, $-\text{NR}^9\text{COR}^9$, $-\text{NHCO}_2\text{R}^9$, $-\text{CO}_2\text{R}^9$, $-\text{CO}_2\text{H}$, $-\text{COR}^9$, $-\text{CONHR}^9$, $-\text{CON}(\text{R}^9)_2$, $-\text{S}(\text{O})_2\text{R}^9$, $-\text{SONH}_2$, $-\text{S}(\text{O})\text{R}^9$, $-\text{SO}_2\text{NHR}^9$, or $-\text{NHS}(\text{O})_2\text{R}^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

51. (new) The compound according to claim 22 wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or
 ii) $\text{CH}_2\text{CO}_2\text{H}$, or an ester, or an amide thereof; or R^2 is an isostere of said $\text{CH}_2\text{CO}_2\text{H}$; and
 wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

52. (new) The compound according to claim 22 wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or
 ii) $\text{CH}_2\text{CO}_2\text{H}$, or an ester, or an amide thereof; or R^2 is an isostere of said $\text{CH}_2\text{CO}_2\text{H}$; and
 wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-\text{R}^9$, $-\text{OR}^9$, $-\text{OH}$, $-\text{SH}$, $-\text{SR}^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-\text{OPh}$, substituted $-\text{OPh}$, $-\text{NO}_2$, $-\text{CN}$, $-\text{NH}_2$, $-\text{NHR}^9$, $-\text{N}(\text{R}^9)_2$, $-\text{NHCOR}^9$, $-\text{NHCONHR}^9$, $-\text{NHCON}(\text{R}^9)_2$, $-\text{NR}^9\text{COR}^9$, $-\text{NHCO}_2\text{R}^9$, $-\text{CO}_2\text{R}^9$, $-\text{CO}_2\text{H}$, $-\text{COR}^9$, $-\text{CONHR}^9$, $-\text{CON}(\text{R}^9)_2$, $-\text{S}(\text{O})_2\text{R}^9$, $-\text{SONH}_2$, $-\text{S}(\text{O})\text{R}^9$, $-\text{SO}_2\text{NHR}^9$, or $-\text{NHS}(\text{O})_2\text{R}^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

53. (new) The compound according to claim 22 wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$, $-CO_2R^9$, $-CO_2H$, $-COR^9$, $-CONHR^9$, $-CON(R^9)_2$, $-S(O)_2R^9$, $-SONH_2$, $-S(O)R^9$, $-SO_2NHR^9$, or $-NHS(O)_2R^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

54. (new) The compound according to claim 22 wherein Z is oxygen; wherein R^1 is hydrogen, $-R$, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$; and wherein R^2 is:

- i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or CH_2CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CH_2CO_2H .

55. (new) The compound according to claim 22 wherein Z is oxygen; wherein R¹ is hydrogen, -R, -CH₂OR, -CH₂SR, or -CH₂Y; and wherein R³ is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

56. (new) The compound according to claim 22 wherein Z is oxygen; wherein R¹ is hydrogen, -R, -CH₂OR, -CH₂SR, or -CH₂Y; and wherein R⁴ and R⁵ taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R⁹, -OR⁹, -OH, -SH, -SR⁹, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO₂, -CN, -NH₂, -NHR⁹, -N(R⁹)₂, -NHCOR⁹, -NHCONHR⁹, -NHCON(R⁹)₂, -NR⁹COR⁹, -NHCO₂R⁹, -CO₂R⁹, -CO₂H, -COR⁹, -CONHR⁹, -CON(R⁹)₂, -S(O)₂R⁹, -SONH₂, -S(O)R⁹, -SO₂NHR⁹, or -NHS(O)₂R⁹; and

wherein each R⁹ is independently selected from an aliphatic group or a substituted aliphatic group.

57. (new) The compound according to claim 22 wherein R^1 is hydrogen, $-R$, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$; wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or

CH_2CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CH_2CO_2H ; and

wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

58. (new) The compound according to claim 22 wherein R^1 is hydrogen, $-R$, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$; wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or

CH_2CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CH_2CO_2H ; and

wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$,

$-\text{CO}_2\text{R}^9$, $-\text{CO}_2\text{H}$, $-\text{COR}^9$, $-\text{CONHR}^9$, $-\text{CON}(\text{R}^9)_2$, $-\text{S}(\text{O})_2\text{R}^9$,
 $-\text{SONH}_2$, $-\text{S}(\text{O})\text{R}^9$, $-\text{SO}_2\text{NHR}^9$, or $-\text{NHS}(\text{O})_2\text{R}^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

59. (new) The compound according to claim 22 wherein R^1 is hydrogen, $-\text{R}$, $-\text{CH}_2\text{OR}$, $-\text{CH}_2\text{SR}$, or $-\text{CH}_2\text{Y}$; wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-\text{R}^9$, $-\text{OR}^9$, $-\text{OH}$, $-\text{SH}$, $-\text{SR}^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-\text{OPh}$, substituted $-\text{OPh}$, $-\text{NO}_2$, $-\text{CN}$, $-\text{NH}_2$, $-\text{NHR}^9$, $-\text{N}(\text{R}^9)_2$, $-\text{NHCOR}^9$, $-\text{NHCONHR}^9$, $-\text{NHCON}(\text{R}^9)_2$, $-\text{NR}^9\text{COR}^9$, $-\text{NHCO}_2\text{R}^9$, $-\text{CO}_2\text{R}^9$, $-\text{CO}_2\text{H}$, $-\text{COR}^9$, $-\text{CONHR}^9$, $-\text{CON}(\text{R}^9)_2$, $-\text{S}(\text{O})_2\text{R}^9$, $-\text{SONH}_2$, $-\text{S}(\text{O})\text{R}^9$, $-\text{SO}_2\text{NHR}^9$, or $-\text{NHS}(\text{O})_2\text{R}^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

60. (new) The compound according to claim 22 wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or

$\text{CH}_2\text{CO}_2\text{H}$, or an ester, or an amide thereof; or R^2 is an isostere of said $\text{CH}_2\text{CO}_2\text{H}$;

wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and
wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-\text{R}^9$, $-\text{OR}^9$, $-\text{OH}$, $-\text{SH}$, $-\text{SR}^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-\text{OPh}$, substituted $-\text{OPh}$, $-\text{NO}_2$, $-\text{CN}$, $-\text{NH}_2$, $-\text{NHR}^9$, $-\text{N}(\text{R}^9)_2$, $-\text{NHCOR}^9$, $-\text{NHCONHR}^9$, $-\text{NHCON}(\text{R}^9)_2$, $-\text{NR}^9\text{COR}^9$, $-\text{NHCO}_2\text{R}^9$, $-\text{CO}_2\text{R}^9$, $-\text{CO}_2\text{H}$, $-\text{COR}^9$, $-\text{CONHR}^9$, $-\text{CON}(\text{R}^9)_2$, $-\text{S}(\text{O})_2\text{R}^9$, $-\text{SONH}_2$, $-\text{S}(\text{O})\text{R}^9$, $-\text{SO}_2\text{NHR}^9$, or $-\text{NHS}(\text{O})_2\text{R}^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

61. (new) The compound according to claim 22 wherein Z is oxygen;

wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or

$\text{CH}_2\text{CO}_2\text{H}$, or an ester, or an amide thereof; or R^2 is an isostere of said $\text{CH}_2\text{CO}_2\text{H}$; and wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

62. (new) The compound according to claim 22 wherein Z is oxygen; wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or

$\text{CH}_2\text{CO}_2\text{H}$, or an ester, or an amide thereof; or R^2 is an isostere of said $\text{CH}_2\text{CO}_2\text{H}$; and

wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-\text{R}^9$, $-\text{OR}^9$, $-\text{OH}$, $-\text{SH}$, $-\text{SR}^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-\text{OPh}$, substituted $-\text{OPh}$, $-\text{NO}_2$, $-\text{CN}$, $-\text{NH}_2$, $-\text{NHR}^9$, $-\text{N}(\text{R}^9)_2$, $-\text{NHCOR}^9$, $-\text{NHCONHR}^9$, $-\text{NHCON}(\text{R}^9)_2$, $-\text{NR}^9\text{COR}^9$, $-\text{NHCO}_2\text{R}^9$, $-\text{CO}_2\text{R}^9$, $-\text{CO}_2\text{H}$, $-\text{COR}^9$, $-\text{CONHR}^9$, $-\text{CON}(\text{R}^9)_2$, $-\text{S}(\text{O})_2\text{R}^9$, $-\text{SONH}_2$, $-\text{S}(\text{O})\text{R}^9$, $-\text{SO}_2\text{NHR}^9$, or $-\text{NHS}(\text{O})_2\text{R}^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

63. (new) The compound according to claim 22 wherein Z is oxygen; wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$, $-CO_2R^9$, $-CO_2H$, $-COR^9$, $-CONHR^9$, $-CON(R^9)_2$, $-S(O)_2R^9$, $-SONH_2$, $-S(O)R^9$, $-SO_2NHR^9$, or $-NHS(O)_2R^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

64. (new) The compound according to claim 22 wherein Z is oxygen; wherein R^1 is hydrogen, $-R$, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$; wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or CH_2CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CH_2CO_2H ; and

wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

65. (new) The compound according to claim 22 wherein Z is oxygen;
wherein R^1 is hydrogen, -R, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$;
wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or

CH_2CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CH_2CO_2H ; and

wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$, $-CO_2R^9$, $-CO_2H$, $-COR^9$, $-CONHR^9$, $-CON(R^9)_2$, $-S(O)_2R^9$, $-SONH_2$, $-S(O)R^9$, $-SO_2NHR^9$, or $-NHS(O)_2R^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

66. (new) The compound according to claim 22 wherein Z is oxygen;
wherein R¹ is hydrogen, -R, -CH₂OR, -CH₂SR, or -CH₂Y;
wherein R³ is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and
wherein R⁴ and R⁵ taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R⁹, -OR⁹, -OH, -SH, -SR⁹, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO₂, -CN, -NH₂, -NHR⁹, -N(R⁹)₂, -NHCOR⁹, -NHCONHR⁹, -NHCON(R⁹)₂, -NR⁹COR⁹, -NHCO₂R⁹, -CO₂R⁹, -CO₂H, -COR⁹, -CONHR⁹, -CON(R⁹)₂, -S(O)₂R⁹, -SONH₂, -S(O)R⁹, -SO₂NHR⁹, or -NHS(O)₂R⁹; and

wherein each R⁹ is independently selected from an aliphatic group or a substituted aliphatic group.

67. (new) The compound according to claim 22 wherein Z is oxygen;
wherein R² is:
i) CO₂H, or an ester, or an amide thereof; or R² is an isostere of said CO₂H; or
CH₂CO₂H, or an ester, or an amide thereof; or R² is an isostere of said CH₂CO₂H;

wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and

wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$, $-CO_2R^9$, $-CO_2H$, $-COR^9$, $-CONHR^9$, $-CON(R^9)_2$, $-S(O)_2R^9$, $-SONH_2$, $-S(O)R^9$, $-SO_2NHR^9$, or $-NHS(O)_2R^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

68. (new) The compound according to claim 22 wherein R^1 is hydrogen, $-R$, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$; wherein R^2 is:

i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or

CH_2CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CH_2CO_2H ;

wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said

heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein R^4 and R^5 taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$, $-CO_2R^9$, $-CO_2H$, $-COR^9$, $-CONHR^9$, $-CON(R^9)_2$, $-S(O)_2R^9$, $-SONH_2$, $-S(O)R^9$, $-SO_2NHR^9$, or $-NHS(O)_2R^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

69. (new) The compound according to claim 22 wherein Z is oxygen; wherein R^1 is hydrogen, $-R$, $-CH_2OR$, $-CH_2SR$, or $-CH_2Y$; wherein R^2 is:

- i) CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CO_2H ; or CH_2CO_2H , or an ester, or an amide thereof; or R^2 is an isostere of said CH_2CO_2H ; and

wherein R^3 is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring

system wherein each ring contains up to three heteroatoms selected from O, N, or S;

wherein R⁴ and R⁵ taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R⁹, -OR⁹, -OH, -SH, -SR⁹, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO₂, -CN, -NH₂, -NHR⁹, -N(R⁹)₂, -NHCOR⁹, -NHCONHR⁹, -NHCON(R⁹)₂, -NR⁹COR⁹, -NHCO₂R⁹, -CO₂R⁹, -CO₂H, -COR⁹, -CONHR⁹, -CON(R⁹)₂, -S(O)₂R⁹, -SONH₂, -S(O)R⁹, -SO₂NHR⁹, or -NHS(O)₂R⁹; and

wherein each R⁹ is independently selected from an aliphatic group or a substituted aliphatic group.

70. (new) The compound according to claim 22 wherein R² is CO₂H.

71. (new) The compound according to claim 22 wherein R¹ is -CH₂OR, -CH₂SR, or -CH₂Y.

72. (new) The compound according to claim 71 wherein R¹ is -CH₂Y.

73. (new) The compound according to claim 72 wherein R¹ is -CH₂F.

74. (new) The compound according to claim 22 wherein R³ is a C₁₋₄ alkyl group.

75. (new) The compound according to claim 22 wherein R¹ is -CH₂F and R³ is a C₁₋₄ alkyl group.

76. (new) The compound according to claim 22 wherein R⁴ and R⁵ taken together with the intervening nitrogen form a ring selected from isoindole, indoline, indazole, purine, dihydropyridine, benzimidazole, imidazole, imidazoline, pyrrole, pyrrolidine, pyrroline, pyrazole, pyrazoline, pyrazolidine, triazole, piperidine, morpholine, thiomorpholine, piperazine, phenothiazine, phenoxazine, dihydrophenazine, dihydrocinnoline, dihydroquinoxaline, tetrahydroquinoline, tetrahydroisoquinoline, dibenzoazepine, dihydro-dibenzoazepine, dihydronaphthyridine, tetrahydronaphthyridine, dihydroacridine, β -carboline, pyrido[4,3-b]indole, 2,3,9-triazafluorene, 9-thia-2,10-diazaanthracene, 3,6,9-triazafluorene, thieno[3,2-b]pyrrole, or dihydrophenanthridine;

wherein said ring is optionally substituted with one or more groups independently selected from halogen, -R⁹, -OR⁹, -OH, -SH, -SR⁹, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO₂, -CN, -NH₂, -NHR⁹, -N(R⁹)₂, -NHCOR⁹, -NHCONHR⁹, -NHCON(R⁹)₂, -NR⁹COR⁹, -NHCO₂R⁹, -CO₂R⁹, -CO₂H, -COR⁹, -CONHR⁹, -CON(R⁹)₂, -S(O)₂R⁹, -SONH₂, -S(O)R⁹, -SO₂NHR⁹, or -NHS(O)₂R⁹; and

wherein each R⁹ is independently selected from an aliphatic group or a substituted aliphatic group.

77. (new) The compound according to claim 76 wherein R⁴ and R⁵ taken together with the intervening

nitrogen form a ring selected from carbazole, phenothiazine, indole, indoline, 5H-dibenzo[b,f]azepine, 10,11-dihydro-5H-dibenzo[b,f]azepine, β -carboline, pyrido[4,3-b]indole, 2,3,9-triazafluorene, 9-thia-2,10-diazaanthracene, 3,6,9-triazafluorene, thieno[3,2-b]pyrrole, or dihydrophenanthridine;

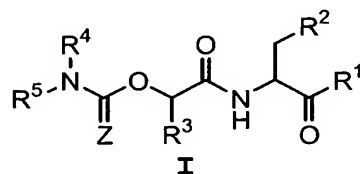
wherein said ring is optionally substituted with one or more groups independently selected from halogen, $-R^9$, $-OR^9$, $-OH$, $-SH$, $-SR^9$, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, $-OPh$, substituted $-OPh$, $-NO_2$, $-CN$, $-NH_2$, $-NHR^9$, $-N(R^9)_2$, $-NHCOR^9$, $-NHCONHR^9$, $-NHCON(R^9)_2$, $-NR^9COR^9$, $-NHCO_2R^9$, $-CO_2R^9$, $-CO_2H$, $-COR^9$, $-CONHR^9$, $-CON(R^9)_2$, $-S(O)_2R^9$, $-SONH_2$, $-S(O)R^9$, $-SO_2NHR^9$, or $-NHS(O)_2R^9$; and

wherein each R^9 is independently selected from an aliphatic group or a substituted aliphatic group.

78. (new) A pharmaceutical composition comprising a compound according to claim 22 and a pharmaceutically acceptable carrier.

79. (new) A method of treating an inflammatory disease, osteoarthritis, rheumatoid arthritis, psoriasis, glomerulonephritis, graft vs host disease, inflammatory bowel disease, sepsis, septic shock, burns, stroke, cerebral ischemia, traumatic brain injury, neurological damage due to stroke, spinal cord injury, amyotrophic lateral sclerosis, multiple sclerosis, myocardial infarct, myocardial ischemia, atherosclerosis, acute respiratory failure, adult respiratory distress syndrome, pancreatitis, various forms of liver and renal disease,

an excess dietary alcohol intake disease, chronic active hepatitis, hepatitis-B, hepatitis-C, coronary artery bypass graft or a treatment for complications associated with coronary bypass grafts in a patient that is alleviated by treatment with a caspase inhibitor, comprising administering to a patient in need of such a treatment a therapeutically effective amount of a compound according to formula I:



80. (new) The method according to claim 79 wherein said method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a compound according to claim 22.

81. (new) A method for the preservation of cells in an organ for transplant or in a blood product said method comprising the step of bathing the cells in a solution of a compound of formula I.